# General

## Guideline Title

Pituitary incidentaloma: an Endocrine Society clinical practice guideline.

## Bibliographic Source(s)

Freda PU, Beckers AM, Katznelson L, Molitch ME, Montori VM, Post KD, Vance ML, Endocrine Society. Pituitary incidentaloma: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2011 Apr;96(4):894-904. [49 references] PubMed

## Guideline Status

This is the current release of the guideline.

# Recommendations

## Major Recommendations

Definitions for the quality of the evidence (+OOO, ++OO, +++O, and ++++); the strength of the recommendation (1 or 2); and the difference between a "recommendation" and a "suggestion" are provided at the end of the "Major Recommendations" field.

Initial Evaluation of a Patient with a Pituitary Incidentaloma

The Task Force recommends that patients presenting with a pituitary incidentaloma undergo a complete history and physical examination that includes evaluations for evidence of hypopituitarism and a hormone hypersecretion syndrome. Patients with evidence of either of these conditions should undergo an appropriately directed biochemical evaluation:

- The Task Force recommends that all patients with a pituitary incidentaloma, including those without symptoms, undergo clinical and laboratory evaluations for hormone hypersecretion (1|+++O).
- The Task Force recommends that patients with a pituitary incidentaloma with or without symptoms also undergo clinical and laboratory evaluations for hypopituitarism (1|+++O).
- The Task Force recommends that all patients presenting with a pituitary incidentaloma abutting the optic nerves or chiasm on magnetic resonance imaging (MRI) undergo a formal visual field (VF) examination (1|++++).
- The Task Force recommends that all patients have a MRI scan, if possible, to evaluate the pituitary incidentaloma (if the incidentaloma was initially only diagnosed by computed tomography [CT] scan) to better delineate the nature and extent of the incidentaloma (1|++++).

Follow-Up Testing of the Pituitary Incidentaloma

Patients with incidentalomas who do not meet criteria for surgical removal of the tumor should receive nonsurgical follow-up (2|++OO) with clinical assessments and the following tests:

- MRI scan of the pituitary 6 months after the initial scan if the incidentaloma is a macroincidentaloma and 1 year after the initial scan if it is a microincidentaloma (1|++OO). In patients whose incidentaloma does not change in size, the Task Force suggests repeating the MRI every year for macroincidentalomas and every 1–2 years in microincidentalomas for the following 3 years, and gradually less frequently thereafter (2|++OO).
- VF testing in patients with a pituitary incidentaloma that enlarges to abut or compress the optic nerves or chiasm on a follow-up imaging study (1|++++). The Task Force suggests that clinicians do not need to test VF in patients whose incidentalomas are not close to the chiasm and who have no new symptoms and are being followed closely by MRI (2|+OOO).
- Clinical and biochemical evaluations for hypopituitarism 6 months after the initial testing and yearly thereafter in patients with a pituitary macroincidentaloma, although typically hypopituitarism develops with the finding of an increase in size of the incidentaloma (1|++OO). The Task Force suggests that clinicians do not need to test for hypopituitarism in patients with pituitary microincidentalomas whose clinical picture, history, and MRI do not change over time (2|++OO).
- Patients who develop any signs or symptoms potentially related to the incidentaloma or who show an increase in size of the incidentaloma on MRI should undergo more frequent or detailed evaluations as indicated clinically (1|++OO).

Indications for Surgical Therapy of the Pituitary Incidentaloma

The Task Force recommends that patients with a pituitary incidentaloma be referred for surgery if they have the following (1|++++):

- A VF deficit due to the lesion
- Other visual abnormalities, such as ophthalmoplegia or neurological compromise due to compression by the lesion
- Lesion abutting or compressing the optic nerves or chiasm on MRI
- Pituitary apoplexy with visual disturbance
- Hypersecreting tumors other than prolactinomas as recommended by other guidelines of The Endocrine Society and The Pituitary Society

The Task Force suggests that surgery be considered for patients with a pituitary incidentaloma if they have the following (2|++OO):

- Clinically significant growth of the pituitary incidentaloma
- Loss of endocrinological function
- A lesion close to the optic chiasm and a plan to become pregnant
- Unremitting headache

Definitions:

Quality of Evidence

+OOO Denotes very low quality evidence

++OO Denotes low quality evidence

+++O Denotes moderate quality evidence

++++ Denotes high quality evidence

Strength of Recommendation

1 - Indicates a strong recommendation and is associated with the phrase "The Task Force recommends."

2 - Denotes a weak recommendation and is associated with the phrase "The Task Force suggests."

## Clinical Algorithm(s)

A flow diagram for the evaluation and treatment of pituitary incidentalomas is provided in the original guideline document.

# Scope

## Disease/Condition(s)

- Pituitary incidentalomas
- Nonfunctioning pituitary adenomas

Note: The guidelines are relevant to all pituitary incidentalomas, those that have the appearance typical of a pituitary adenoma as well as cystic lesions. By convention, microincidentalomas are less than 1 cm and macroincidentalomas are at least 1 cm in size.

## Guideline Category

Evaluation

Management

Treatment

## Clinical Specialty

Endocrinology

Neurological Surgery

## Intended Users

Physicians

## Guideline Objective(s)

To formulate practice guidelines for endocrine evaluation and treatment of pituitary incidentalomas

## Target Population

Adults with pituitary incidentalomas

## Interventions and Practices Considered

Evaluation/Management

1. Clinical and laboratory evaluations for hormone hypersecretion
2. Clinical and laboratory evaluations for hypopituitarism
3. Visual field examination
4. Magnetic resonance imaging (MRI) scan
5. Non-surgical follow-up in patients not meeting criteria for surgical removal
6. Referral for surgery

## Major Outcomes Considered

- Change in size of pituitary incidentaloma
- Development of visual field defects
- Neurological deficits
- Alteration of pituitary function
- Pituitary apoplexy
- Mortality

# Methodology

## Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

## Description of Methods Used to Collect/Select the Evidence

The Endocrine Society's Task Force commissioned one systematic review (see the "Availability of Companion Documents" field) to support their guidelines on nonfunctioning pituitary adenomas (NFPAs) and pituitary incidentalomas (PIs).

Eligibility Criteria

Eligible studies were longitudinal observational cohort studies that enrolled patients with PIs/NFPAs and followed them up without any treatment from the time of detection. The outcomes of interest in this systematic review are change in size; development of visual field defects, neurological deficits, alteration of pituitary function, pituitary apoplexy, and mortality. The reviewers excluded case reports or cross-sectional studies with no longitudinal follow-up and those with follow-up less than 1 year.

Study Identification

An expert reference librarian conducted the electronic search with input from study investigators with expertise in systematic reviews. The reviewers searched MEDLINE, EMBASE, and Cochrane CENTRAL electronic databases from 1966 through February 2009. The detailed strategy is available in the Supplemental Appendix, published on The Endocrine Society's Journals Online web site at http://jcem.endojournals.org . To identify additional candidate studies, the reviewers reviewed the reference lists of the eligible primary studies, narrative reviews, and systematic reviews; and they queried the expert members of the commissioning task force.

Study Selection

Working independently and in duplicate, reviewers screened all abstracts and titles. After obtaining all potentially eligible studies in full text, these reviewers, again working independently and in duplicate, determined eligibility with acceptable chance-adjusted agreement (mean kappa = 0.80). Disagreements were resolved by consensus or arbitration.

## Number of Source Documents

The search identified 1069 candidate references, of which 13 studies described in 14 publications were deemed eligible. The reviewers found one additional unpublished study by contacting experts in the field. They excluded three studies because the case identification was done using older computed tomography (CT) scan techniques that were not comparable with current magnetic resonance imaging (MRI) studies and due to the lack of sufficient data for meta-analysis, making the total number of included studies 11.

## Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

## Rating Scheme for the Strength of the Evidence

Quality of Evidence

+OOO Denotes very low quality evidence

++OO Denotes low quality evidence

+++O Denotes moderate quality evidence

++++ Denotes high quality evidence

## Methods Used to Analyze the Evidence

Meta-Analysis of Randomized Controlled Trials

Systematic Review with Evidence Tables

## Description of the Methods Used to Analyze the Evidence

The Endocrine Society's Task Force commissioned one systematic review (see the "Availability of Companion Documents" field) to support their guidelines on nonfunctioning pituitary adenomas (NFPAs) and pituitary incidentalomas (PIs).

Data Collection

Using a standardized, piloted, and web-based data extraction form and working in duplicate, the reviewers abstracted the following descriptive data from each study: description of study characteristics and participants (age, sex, hormonal and visual function at baseline, percentage of macroadenomas, geographical origin, period of inclusion, and length of follow-up). They extracted the outcomes of interest at the longest point of complete follow-up. They contacted authors for missing data when needed.

Quality Assessment

The reviewers used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach to rate the quality of evidence, i.e., the extent to which they can be confident in the estimates with the purpose of making recommendations. To assess the methodological quality of the studies, they determined how the cohorts were selected, whether there was a follow-up protocol and the extent of loss to follow-up, and how outcomes were ascertained. They also noted how each study defined the increase in tumor size.

Metaanalyses

The reviewers estimated from each study the event rate per 100 person-years (PYs) and associated 95% confidence interval (CI) and pooled using the DerSimonian and Laird random-effects model. They quantified inconsistency using the $I^2$ statistic, which describes the proportion of heterogeneity across studies that is not due to chance, thus describing the extent of true inconsistency in results across trials. $I^2$ less than 25% and $I^2$ greater than 50% reflect small and large inconsistency, respectively.

Subgroup and Sensitivity Analyses

To explore causes of inconsistency and subgroup-treatment interactions, subgroup analyses were specified *a priori* according to the following factors: tumor size at presentation (microadenoma *vs*. macroadenoma with cutoff defined at 10 mm), tumor characteristics on imaging (solid vs. cystic), patient's sex and age (younger than 65 years vs. older). A test of interaction was used to explore subgroup effects. Sensitivity analysis was planned to determine whether the exclusion of borderline eligible studies or unpublished studies would affect study conclusions.

## Methods Used to Formulate the Recommendations

Expert Consensus

## Description of Methods Used to Formulate the Recommendations

The Task Force consisted of a chair, selected by the Clinical Guidelines Subcommittee of The Endocrine Society, five additional experts, a methodologist, and a medical writer.

Consensus was guided by systematic reviews of evidence and discussions through a series of conference calls and e-mails and one in-person meeting. An initial draft guideline was prepared by the Task Force, with the help of a medical writer, and reviewed and commented on by members of The Endocrine Society and the European Society of Endocrinology. A second draft was reviewed and approved by The Endocrine

Society Council. At each stage of review, the Task Force received written comments and incorporated substantive changes.

### Rating Scheme for the Strength of the Recommendations

Strength of Recommendation

1 - Indicates a strong recommendation and is associated with the phrase "The Task Force recommends."

2 - Denotes a weak recommendation and is associated with the phrase "The Task Force suggests."

### Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

### Method of Guideline Validation

External Peer Review

Internal Peer Review

### Description of Method of Guideline Validation

An initial draft guideline was prepared by the Task Force, with the help of a medical writer, and reviewed and commented on by members of The Endocrine Society and the European Society of Endocrinology. A second draft was reviewed and approved by The Endocrine Society Council. At each stage of review, the Task Force received written comments and incorporated substantive changes.

## Evidence Supporting the Recommendations

### Type of Evidence Supporting the Recommendations

The type of supporting evidence is specifically stated for most recommendations (see the "Major Recommendations" field).

## Benefits/Harms of Implementing the Guideline Recommendations

### Potential Benefits

- Accurate identification of hormone hypersecretion and hypopituitarism
- Early detection of a growth hormone (GH)-secreting tumor, which would likely be asymptomatic, could reduce long-term morbidity and increase the likelihood of surgical cure.
- Some patients planning pregnancy may benefit from surgery if their tumor is close to the optic chiasm because there is a small risk that lactotroph hyperplasia in the normal gland may lead to tumor compression of the optic nerve or chiasm, and closer follow-up in such patients should be undertaken.

### Potential Harms

- Costs and burden of potentially unnecessary testing
- False-positive rate and low rate of true-positive testing
- Surgical interventions have associated morbidities and costs.

# Qualifying Statements

## Qualifying Statements

- Clinical Practice Guidelines are developed to be of assistance to endocrinologists and other health care professionals by providing guidance and recommendations for particular areas of practice. The Guidelines should not be considered inclusive of all proper approaches or methods, or exclusive of others. The Guidelines cannot guarantee any specific outcome, nor do they establish a standard of care. The Guidelines are not intended to dictate the treatment of a particular patient. Treatment decisions must be made based on the independent judgment of health care providers and each patient's individual circumstances.
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# Implementation of the Guideline

## Description of Implementation Strategy

An implementation strategy was not provided.

## Implementation Tools

Clinical Algorithm

Patient Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

# Institute of Medicine (IOM) National Healthcare Quality Report Categories

## IOM Care Need

Getting Better

## IOM Domain

Effectiveness

# Identifying Information and Availability

## Bibliographic Source(s)

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## Adaptation

Not applicable: The guideline was not adapted from another source.

## Date Released

2011 Apr

## Guideline Developer(s)

The Endocrine Society - Professional Association

## Source(s) of Funding

The Endocrine Society

The Task Force received no corporate funding or remuneration.

## Guideline Committee

Pituitary Incidentaloma Task Force

## Composition of Group That Authored the Guideline

*Task Force Members*: Pamela U. Freda; Albert M. Beckers; Laurence Katznelson; Mark E . Molitch; Victor M. Montori; Kalmon D. Post; Mary Lee Vance

## Financial Disclosures/Conflicts of Interest

Pamela U. Freda, M.D.—Financial or Business/Organizational Interests: Novartis, Ipsen, and Pfizer; Significant Financial Interest or Leadership Position: none declared.

Albert M. Beckers, M.D., D.Sc., Ph.D.—Financial or Business/Organizational Interests: Novartis, Ipsen, and Pfizer; Significant Financial Interest or Leadership Position: none declared.

Laurence Katznelson, M.D.—Financial or Business/Organizational Interests: Novartis, Ipsen, and Novo Nordisk; Significant Financial Interest or Leadership Position: none declared.

Mark E. Molitch, M.D.—Financial or Business/Organizational Interests: Tercica/Ipsen, Novartis; Significant Financial Interest or Leadership Position: none declared.

Victor M. Montori, M.D.*—Financial or Business/Organizational Interests: KER Unit (Mayo Clinic); Significant Financial Interest or Leadership Position: none declared.

Kalmon D. Post, M.D.—Financial or Business/Organizational Interests: none declared; Significant Financial Interest or Leadership Position: none declared.

Mary Lee Vance, M.D.—Financial or Business/Organizational Interests: Novartis; Significant Financial Interest or Leadership Position: none declared.

*Evidence-based reviews for this guideline were prepared under contract with The Endocrine Society.

## Guideline Endorser(s)

## Guideline Status

This is the current release of the guideline.

## Guideline Availability

Electronic copies: Available in Portable Document Format (PDF) from The Endocrine Society Web site .

Print copies: Available from The Endocrine Society, Phone: (301) 941.0210; Email: Societyservices@endo-society.org

## Availability of Companion Documents

The following is available:

- Fernández-Balsells MM, Murad MH, Barwise A, Gallegos-Orozco JF, Paul A, Lane MA, Lampropulos JF, Natividad I, Perestelo-Pérez L, Ponce de León-Lovatón PG, Erwin PJ, Carey J, Montori VM. Natural history of nonfunctioning pituitary adenomas and incidentalomas: a systematic review and metaanalysis. J Clin Endocrinol Metab 2011 Apr;96(4):905-12. Electronic copies: Available to subscribers from the Journal of Clinical Endocrinology & Metabolism Web site .

Print copies: Address all correspondence and requests for reprints to: M. Hassan Murad, M.D., M.P.H., Mayo Clinic, The Knowledge and Encounter Research Unit, 200 First Street SW, Rochester, Minnesota 55905. E-mail: murad.mohammad@mayo.edu.

## Patient Resources

The following is available:

- Patient guide to pituitary incidentaloma assessment and treatment. The Hormone Foundation. 2011 Apr. 2 p. Electronic copies: Available from The Hormone Foundation Web site .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

## NGC Status

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